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No Difference in Cardiac Event-Free Survival Between Positron Emission Tomography-Guided and Single-Photon Emission Computed Tomography-Guided Patient Management

A Prospective, Randomized Comparison of Patients With Suspicion of Jeopardized Myocardium

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OBJECTIVES We sought to prospectively compare nitrogen-13 (^{13}N)-ammonia/^{18}fluorodeoxyglucose (^{18}FDG) positron emission tomography (PET)–guided management with stress/rest technetium-99m (^{99m}Tc)-sestamibi single-photon emission computed tomography (SPECT)–guided management.

BACKGROUND Patients with evidence of jeopardized (i.e., ischemic or viable) myocardium may benefit from revascularization, whereas patients without it should be treated with drugs. Both PET and SPECT imaging have been proven to delineate jeopardized myocardium. When patient management is based on identification of jeopardized myocardium, it is unknown which technique is most accurate for long-term prognosis.

METHODS In a clinical setting, 103 patients considered for revascularization with left ventricular wall motion abnormalities and suspicion of jeopardized myocardium underwent both PET and SPECT imaging. The imaging results were used in a randomized fashion to determine management (percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft surgery [CABG] or drug treatment). Follow-up for cardiac events (cardiac death, myocardial infarction and revascularization) was recorded for 28 ± 1 months. The study was designed to have a power of 80% to detect a 20% difference in the event rate between PET- and SPECT-based management.

RESULTS Management decisions in 49 patients randomized to PET (12 who had PTCA, 14 CABG and 23 drug therapy) were comparable with 54 patients randomized to SPECT (15 who had PTCA, 13 CABG and 26 drug therapy). In terms of cardiac event-free survival, no differences between PET and SPECT were observed (11 vs. 13 cardiac events for PET and SPECT, respectively; p = NS by the Kaplan-Meier statistic).

CONCLUSIONS No difference in patient management or cardiac event-free survival was demonstrated between management based on ^{13}N-ammonia/^{18}FDG PET and that based on stress/rest ^{99m}Tc-sestamibi SPECT imaging. Both techniques may be used for management of patients considered for revascularization with suspicion of jeopardized myocardium. (J Am Coll Cardiol 2001;37:81–8) © 2001 by the American College of Cardiology

Revascularization management in patients with coronary artery disease is an important clinical issue, and assessment of jeopardized (i.e., ischemic or viable) myocardium before revascularization allows prediction of regional and global left ventricular function improvement. Several nuclear myocardial imaging techniques with different radiopharmaceutical agents—thallium-201 (^{201}Tl) (1–4), technetium-99m (^{99m}Tc)-sestamibi (5–7) and ^{18}fluorodeoxyglucose (^{18}FDG) (3,8–21)—dobutamine stress echocardiography (3,22–25) and magnetic resonance imaging (26,27) are used to detect myocardium that could benefit from revascularization. For all of these imaging modalities, varying sensitivities and specificities for postrevascularization recovery of left ventricular function have been reported in an analysis of pooled

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
ECG = electrocardiogram
^{18}FDG = ^{18}fluorodeoxyglucose
^{13}N = nitrogen-13
PET = positron emission tomography
PTCA = percutaneous transluminal coronary angioplasty
SPECT = single-photon emission computed tomography
^{99m}Tc = technetium-99m
^{201}Tl = thallium-201

data (28). Among these techniques, ^{18}FDG positron emission tomographic (PET) imaging is believed to be most accurate by demonstrating high sensitivity and specificity values.

However, from the clinical point of view, long-term prognosis is also important. Several studies have indicated that patients with evidence of jeopardized myocardium benefit from revascularization for prognosis (12–15,29,30), but that similar patients who are only treated with drugs have a high risk for future cardiac events (13–15). Moreover, patients without signs of jeopardized myocardium appear to be at increased risk of perioperative complications and should continue drug treatment (12). These data suggest that jeopardized myocardium should be revascularized for prognostic reasons. However, most studies addressing prognosis in jeopardized myocardium are small and retrospective and do not include a comparison with other viability assessment techniques.

To date, it is unknown which technique is most accurate for determination of patient management and for long-term prognosis when management is based on identification of jeopardized myocardium. In the current study, we examined in a prospective, blinded, randomized fashion, the impact of nitrogen-13 (^{13}N)-ammonia/^{18}FDG PET–guided management and stress/rest ^{99m}Tc-sestamibi single-photon emission computed tomographic (SPECT) imaging–guided management (percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft surgery [CABG] or drug treatment) on cardiac event-free survival. All patients included in the study were potential candidates for revascularization, and in all patients, assessment of jeopardized (i.e., ischemic or viable) myocardium was indicated.

METHODS

Patient selection. The study group was recruited from patients referred for routine diagnostic coronary angiography for clinical reasons (e.g., angina, myocardial ischemia, arrhythmias, heart failure) and in whom a revascularization procedure was considered. In our institution, coronary angiography results and clinical data are discussed on a daily basis by the revascularization team of the Thorax Center. This team consists of a thoracic surgeon, an invasive cardiologist, the patients' cardiologist and a nuclear cardiologist, and they determine patient management (i.e., CABG, PTCA or drug treatment). Patients were eligible for the present study if, as a result of the revascularization team discussion, additional information was needed regarding the amount or the absence of jeopardized myocardium in an area exhibiting wall motion abnormalities supplied by a coronary artery with significant (>50%) stenosis. In the eligible patients, the amount of jeopardized myocardium had to have an impact on patient management (PTCA, CABG or drug treatment), and a revascularization procedure had to be technically feasible by demonstrating adequate target vessels. Furthermore, the patients' clinical condition had to permit protocol participation. Patients <20 years old and >80 years old, patients with unstable angina and patients with recent (<4 weeks) myocardial infarction were excluded. If they met all of the aforementioned criteria, patients were candidates for scintigraphic evaluation.

The study was approved by the Institutional Review Board of the University Hospital Groningen, and 112 patients were included. When informed, written consent was obtained, patients underwent an interview, physical examination, routine laboratory investigation and echocardiography for assessment of left ventricular function. A history of myocardial infarction was documented either by clinical history or pathologic Q waves on the rest electrocardiogram (ECG). Baseline New York Heart Association functional class was assessed on the basis of exercise tolerance for angina or heart failure symptoms. Then patients were referred to the Department of Nuclear Medicine and to the PET Center and underwent both stress/rest ^{99m}Tc-sestamibi SPECT and ^{13}N-ammonia/^{18}FDG PET imaging.

SPECT. Stress/rest ^{99m}Tc-sestamibi SPECT myocardial imaging was done using a two-day protocol. Stress imaging was performed after patients had discontinued vasoactive medication for five plasma half-lives and had refrained from caffeinated beverages for a minimum of 12 h before the studies. For stress imaging, infusion of dipyridamole (0.56 mg/kg body weight in 4 min) was used, and 600 MBq of ^{99m}Tc-sestamibi was injected 6 min after the start of dipyridamole infusion. Imaging started after 60 min. Three days later, rest imaging was performed 60 min after 600 MBq of ^{99m}Tc-sestamibi was injected at rest. Imaging was performed using a Siemens Orbiter single-head gamma camera (Siemens Gammasonics Inc., Des Plaines, Illinois) equipped with a low energy, high resolution collimator. A 15% window was set over the 140-KeV photon peak. Sixty-four projection images were obtained in the supine position in a 180° arc, imaging for 20 s/view. All images were acquired on a computer in a 64 × 64 matrix (word mode) and stored on an optical disk. The images were reconstructed and corrected for uniformity and center of rotation offset. No attenuation or scatter correction was applied. The images were prefiltered with a two-dimensional Butterworth filter, with an order equal to 6. The cutoff frequency was 0.5. After ramp-filtered back-

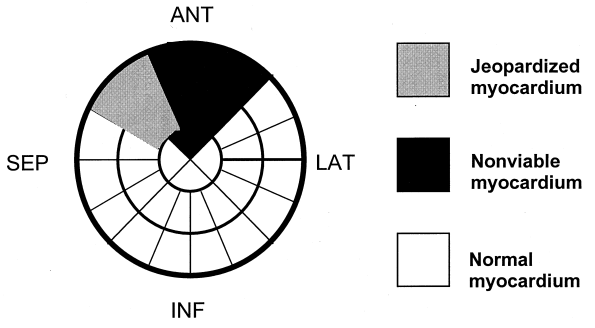

Figure 1. Example of a uniform, blinded polar map consisting of a frame in which areas of jeopardized and nonviable myocardium could be depicted by using a computer. A separate polar map was created for PET results and SPECT results by different physicians. After randomization, only the polar map of the technique which the patient was randomized to receive was presented to the clinicians, who subsequently determined treatment. By using this uniform polar map design, the clinicians were completely unaware whether the polar map showed PET or SPECT results. ANT = anterior; INF = inferior; LAT = lateral; SEP = septal.

projection, slices of two pixels were generated. Slices were reoriented according to the anatomic axis of the heart. Reconstructed slices were displayed as short-axis slices and horizontal and vertical long-axis slices. Analysis was done using the ICON software (Siemens Medical Systems, Hoffman Estates, Illinois). Unprocessed planar images were displayed in the cine format to exclude significant patient motion or breast or diaphragmatic attenuation. Displayed short-axis slices, as well as horizontal long-axis and vertical long-axis slices, were then normalized to the maximal tracer uptake in the heart and shown in color scale for semiquantitative analysis, and polar maps for rest and stress images were reconstructed. The images were analyzed by two experienced readers who reached a consensus reading. The following classification was used: normal myocardium; jeopardized myocardium (>10% reversibility or rest activity ≥50% of maximal activity); and nonviable myocardium (lowest activity in the defect ≤50% of maximal activity and ≤10% reversibility) (7,31,32). According to these criteria, the physicians of the Nuclear Medicine Department depicted regions exhibiting normal, nonviable and jeopardized myocardium in a uniform, blinded polar map (Fig. 1), which was sent to the Trial Coordination Center.

PET. Patients underwent dynamic ^{13}N-ammonia dipyridamole and ^{18}FDG PET imaging using a one-day protocol, as described previously (33). Briefly, PET studies were performed after patients had discontinued vasoactive medication for five plasma half-lives and had refrained from caffeinated beverages for a minimum of 12 h before the studies. Imaging was performed in the supine position with a Siemens ECAT 951 positron camera (Siemens CTI, Knoxville Tennessee), measuring 31 planes simultaneously over 10.8 cm. Measured resolution of the system was 6 mm at full width half maximum. Data were automatically corrected for accidental coincidence and dead time. Patients were positioned with the help of a rectilinear scan. Photon attenuation was measured using a retractable external ring source filled with germanium-68/gallium-68. Dipyridamole perfusion imaging was performed infusing dipyridamole (0.56 mg/kg in 4 min). Imaging was started by injecting 370 MBq of ^{13}N-ammonia 6 min after the start of dipyridamole infusion and continued for 15 min (frames: 12 × 10 s, 1 × 2 min, 1 × 4 min, 1 × 7 min). To stimulate ^{18}FDG uptake, patients were given 75 g of glucose orally before the scanning procedure, and in diabetic patients, ^{18}FDG imaging was done with the hyperinsulinemic euglycemic glucose clamp technique (34). Imaging with ^{18}FDG was performed after injection of 185 MBq of ^{18}FDG and continued for 55 min (frames: 8 × 15 s, 4 × 30 s, 1 × 1 min, 1 × 5 min, 1 × 10 min, 1 × 15 min, 1 × 20 min). Data processing and analysis to detect normal, jeopardized myocardium (mismatch) and nonviable myocardium (match) were performed as described previously (33). Then physicians from the PET Center depicted regions exhibiting normal, nonviable and jeopardized myocardium in a uniform, blinded polar map (Fig. 1), which was sent to the Trial Coordination Center.

Randomization. At the Trial Coordination Center, patients were randomized to receive either ^{13}N-ammonia/^{18}FDG PET or ^{99m}Tc-sestamibi SPECT, for determination of patient management. Weighted randomization was performed on the basis of gender, age and single-vessel or multivessel disease.

Patient management. After randomization, only the uniformly blinded polar map depicting the results of the technique which the patient had been randomized to receive was given by the Trial Coordination Center to the revascularization team of the Thorax Center. By using this uniform polar map, the revascularization team was completely unaware of the information; they did not know whether the polar map showed PET or SPECT results. The results of the nonrandomized polar map were not shown to the revascularization team. For the second time, the team discussed the coronary angiography, ventriculography and clinical data, but this time with the requested scintigraphic results of the tests on jeopardized, nonviable and normal myocardium. For revascularization, our regular criteria were applied and included the presence of at least 20% jeopardized myocardium in the region supplied by a coronary artery with stenosis (>50%). This cutoff value has recently been reported to accurately predict functional improvement of left ventricular function (17). Depending on the results depicted in the blinded polar map and according to the revascularization criteria, the team decided to perform revascularization (CABG or PTCA) or to continue drug treatment. Bypass surgery or PTCA was then performed according to the regular urgency-based schedule, and complete revascularization was attempted in all revascularized patients. After the revascularization procedure, daily ECGs and cardiac enzyme studies were obtained to identify new ST segment elevation or Q-waves associated with an increase in cardiac enzymes, consistent with significant periprocedural myocardial infarction.

Follow-up. Six months later, patients visited the outpatient clinic, where information on clinical events was obtained. Information on survival status and clinical events was again obtained by use of a detailed questionnaire to the patient's cardiologist or general practitioner, or by review of hospital records at 28 ± 1 months after randomization (median 28 months, maximum 46 months).

End points. The end point in this study was cardiac event-free survival during follow-up, starting at randomization. Cardiac events included cardiac death, myocardial infarction and unintended revascularization. Cardiac death was defined as sudden death, death after the onset of symptoms suggestive of cardiac ischemia and death due to heart failure. Noncardiac death was defined as death due to all other causes. Myocardial infarction was defined as an increase in cardiac enzymes or new pathologic Q-waves on the ECG, or both. Unintended revascularization was defined as PTCA or CABG performed due to worsening of the patient's clinical condition, rather than the PTCA or CABG assigned by the revascularization team when patient management was determined.

Statistics. On the basis of previous data from a comparative study using ^{18}FDG PET and stress-redistribution ^{201}Tl imaging, performed by Tamaki et al. (16), we expected a total event rate of 20%. Presuming a 20% higher cardiac event rate for patients randomized to SPECT, we estimated that our sample size had to include at least 95 patients to obtain a power of 80%. To compensate for patient withdrawal, we included 112 patients. Changes within groups were assessed using the paired Student *t* test or the Wilcoxon signed-rank test. Groups were compared by using the Student *t* test or the Wilcoxon two-sample test, as appropriate. According to the intention-to-treat principle, cardiac event-free survival was analyzed with the first cardiac event per patient, using the Kaplan-Meier and log-rank statistic. To determine the subgroups of patients that may benefit from ^{13}N-ammonia/^{18}FDG PET or ^{99m}Tc-sestamibi SPECT, multiple Cox regression analysis was performed on the first occurrence of a cardiac event for all baseline variables. For statistical analysis, SAS version 6.12 (Cary, North Carolina) was used. All data are expressed as the mean value ± SEM. All p values were two-sided, and $p < 0.05$ was considered significant.

RESULTS

Baseline characteristics. Of the 112 study patients, 103 were randomized and nine were not (one patient died, three withdrew from the study, one had a failed PET scan and four had progressive disease requiring treatment before randomization). The patients' baseline characteristics are summarized in Table 1. The patients were characterized by echocardiographic left ventricular ejection fraction >30% or ≤30%. There were no differences in baseline characteristics or medical history between the group randomized to ^{13}N-ammonia/^{18}FDG PET and the group randomized to ^{99m}Tc-sestamibi SPECT.

Table 1. Baseline Characteristics

	PET Group (n = 49)	SPECT Group (n = 54)
Age (years)	62 ± 2	63 ± 1
Vessel disease (1:>1)	13 (27)/36 (73)	12 (22)/42 (78)
Gender (male/female)	40 (82)/9 (18)	49 (91)/5 (9)
NYHA functional class	2.5 ± 0.08	2.3 ± 0.11
Ejection fraction (≤30%/>30%)	17 (35)/32 (65)	19 (35)/35 (65)
Weight (kg)	80.4 ± 1.6	81.9 ± 1.5
Height (m)	1.74 ± 0.01	1.76 ± 0.01
Previous MI	44 (90)	49 (91)
Previous PTCA	12 (24)	11 (20)
Previous CABG	14 (29)	15 (28)
Diabetes mellitus	9 (18)	6 (11)
Hypercholesterolemia	17 (35)	21 (39)
Hypertension	17 (35)	13 (25)
Family history of CAD	21 (43)	28 (52)

Continue variables are expressed as the mean value ± SEM; categoric variables are expressed as the number (%) of the patients in the randomized group.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; MI = myocardial infarction; NHYA = New York Heart Association; PET = positron emission tomography; PTCA = percutaneous transluminal coronary angioplasty; SPECT = single-photon emission computed tomography.

Scintigraphic results. The prevalence of the mean amount of normal, nonviable and jeopardized myocardium was not different between the 103 PET and 103 SPECT images. Positron emission tomography exhibited 68% normal, 16% nonviable and 16% jeopardized myocardium, whereas SPECT exhibited 64% normal, 20% nonviable and 16% jeopardized myocardium.

Treatment. Intended treatment, as determined by the revascularization team, was not different between the PET and SPECT groups (PET: 12 patients had PTCA, 14 had CABG and 23 had drug therapy; SPECT: 15 patients had PTCA, 13 had CABG and 26 had drug therapy). Two patients died before they received their intended treatment: one patient randomized to PET experienced untreatable ventricular fibrillation, and one patient randomized to SPECT experienced sudden death. Before initiation of treatment, no events occurred in other patients. Although the treating clinicians decided that one patient randomized to PET and five patients randomized to SPECT could not receive the intended treatment, the received treatment (PET: 11 patients had PTCA, 13 had CABG and 24 had drug therapy; SPECT: 10 patients had PTCA, 13 had CABG and 30 had drug therapy) did not significantly differ from the intended treatment. In these patients, the intended treatment was not effectuated, because in one patient CABG was not performed due to worsening clinical condition (not allowing a surgical intervention; the patient had to be treated with drugs), in three patients PTCA was not performed because the patients had been stabilized on drugs while waiting for the intended revascularization procedure, one patient refused to undergo PTCA and one patient received CABG instead of PTCA because of technical anatomic reasons. Notably, the treating physicians who

Table 2. First Cardiac Event per Patient After Randomization

	PET Group (n = 49)			SPECT Group (n = 54)					
Events	PTCA (n = 12)	CABG (n = 14)	Intended Drugs (n = 23)	Treatment PTCA (n = 15)	CABG (n = 13)	Drugs (n = 26)	PET Total	SPECT Total	p Value
PTCA	0	1	0	2	0	2	1	4	NS
CABG	1	1	2	2	2	1	4	5	NS
MI	0	0	2	0	1	2	2	3	NS
Cardiac death	2	1	1	0	1	0	4	1	NS

Data are presented as number of patients.
Abbreviations as in Table 1.

decided that patients should not receive their intended treatment did not know whether the PET or SPECT results were used for determination of patient management.

The time from randomization to the second discussion by the revascularization team was not different between the ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT groups (35 ± 3 vs. 40 ± 3 days for PET and SPECT, respectively), and neither was the time from the second discussion to CABG or PTCA (80 ± 19 vs. 92 ± 19 days for PET and SPECT, respectively).

Cardiac events during follow-up. One patient was lost during follow-up. The mean follow-up time from randomization was not different for patients randomized to ^{13}N-ammonia/^{18}FDG PET or ^{99m}Tc-sestamibi SPECT (26 ± 1 vs. 29 ± 1 months [median 28 vs. 29] for PET and SPECT, respectively). Three periprocedural cardiac events were observed: one patient experienced occlusion of the coronary artery after PTCA and had subsequent myocardial infarction; one patient died during CABG; and one patient had a perioperative myocardial infarction. All first cardiac events after randomization are shown in Table 2, and there was no difference in the occurrence of the first cardiac event between the ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT groups, as illustrated by the Kaplan-Meier plot in Figure 2. No difference could be demonstrated in cardiac events between the ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT groups for patients assigned to be revascularized and those assigned to drug treatment (Fig. 3 and 4). No difference was found between the ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT groups for the patients with an ejection fraction ≤30% and >30%. Furthermore, no significant differences were observed for noncardiac death (due to rectum carcinoma, cerebrovascular accident, diabetic coma or pulmonary embolism; 3 vs. 1), hospital admission for heart failure (8 vs. 6) or hospital admission for unstable angina (8 vs. 12) for the PET and SPECT groups, respectively. Multivariate analysis revealed no subgroups that might benefit from ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT in terms of cardiac event-free survival.

DISCUSSION

The present study is the first prospective, randomized study, to our knowledge, addressing the impact of ^{13}N-ammonia/^{18}FDG PET imaging, as compared with stress/rest ^{99m}Tc-sestamibi SPECT imaging, on patient management and long-term prognosis in patients who are candidates for revascularization with suspicion of jeopardized myocardium. We demonstrated that treatment based on assessment of jeopardized myocardium with ^{13}N-ammonia/^{18}FDG PET did not result in differences in patient management and, more importantly, in cardiac event-free survival, as compared with treatment based on ^{99m}Tc-sestamibi SPECT imaging. Furthermore, for both ^{13}N-ammonia/^{18}FDG

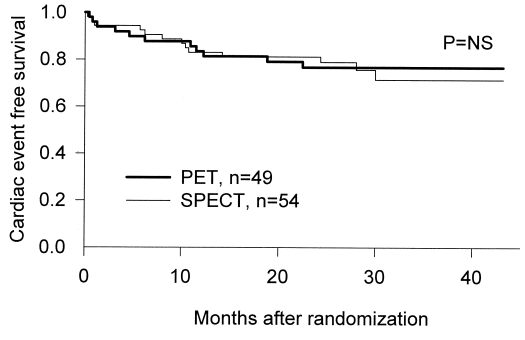

Figure 2. Kaplan-Meier cardiac event-free survival curves for patients randomized to ^{13}N-ammonia/^{18}FDG PET or stress/rest ^{99m}Tc-sestamibi SPECT-based management (PTCA, CABG or drug therapy). All patients were potential candidates for revascularization, and in all patients, assessment of jeopardized myocardium was indicated. CABG = coronary artery bypass graft surgery; ^{18}FDG = ^{18}fluorodeoxyglucose; PET = positron emission tomography; PTCA = percutaneous transluminal angioplasty; SPECT = single-photon emission computed tomography.

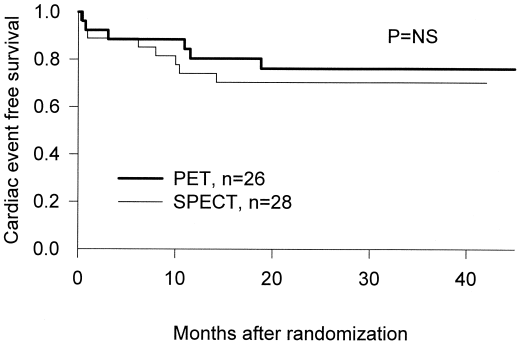

Figure 3. Kaplan-Meier cardiac event-free survival curves for patients intended to undergo revascularization on the basis of ^{13}N-ammonia/^{18}FDG PET or stress/rest ^{99m}Tc-sestamibi SPECT imaging. CABG = coronary artery bypass graft surgery; ^{18}FDG = ^{18}fluorodeoxyglucose; PET = positron emission tomography; PTCA = percutaneous transluminal angioplasty; SPECT = single-photon emission computed tomography.

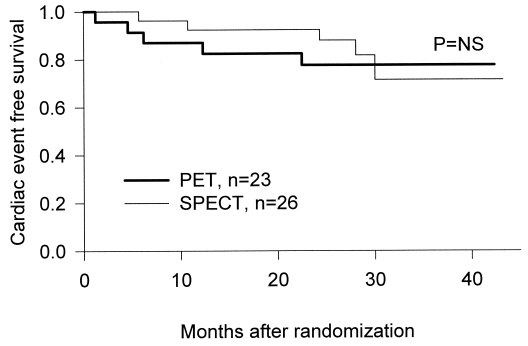

Figure 4. Kaplan-Meier cardiac event-free survival curves for patients intended to be treated with drugs on the basis of ^{13}N-ammonia/^{18}FDG PET or stress/rest ^{99m}Tc-sestamibi SPECT imaging.

PET-guided management and ^{99m}Tc-sestamibi SPECT imaging-guided management, the number of cardiac events was comparable for patients assigned to revascularization and those assigned to drug therapy. No specific subgroups benefiting from either ^{13}N-ammonia/^{18}FDG PET-guided management or ^{99m}Tc-sestamibi SPECT-guided management could be identified in terms of cardiac event-free survival.

Nitrogen-13–ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT. In clinical practice, identification of patients who may benefit from revascularization is an important issue. To date, only nonrandomized and mostly retrospective studies have been performed to evaluate patient management and prognosis based on viability assessment (12–16), but in none of these studies was the revascularization team blinded to the nuclear technique on which patient management was determined. Consequently, a bias for referral to revascularization or drug treatment could have existed. Nevertheless, these studies suggest that when jeopardized myocardium is present, revascularization may result in a better prognosis than drug treatment. Therefore, treatment based on the presence or absence of jeopardized myocardium appears critically important, and in our opinion, this should be the cornerstone of revascularization management in clinical practice.

Both ^{13}N-ammonia/^{18}FDG PET imaging and ^{99m}Tc-sestamibi SPECT imaging are able to identify patients with jeopardized myocardium who may benefit from revascularization in terms of clinical outcome (12–15) and postrevascularization recovery of left ventricular function (3,5–21). However, ^{99m}Tc-sestamibi SPECT imaging is thought to be less accurate for detection of viability, as preserved ^{18}FDG uptake was demonstrated in ^{99m}Tc-sestamibi defects (35–37). Whether ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT imaging have a different impact on prognosis and patient management is unknown. The present study addresses this specific issue and demonstrates that in clinical patient management, the use of the specific viability tracer ^{18}FDG combined with ^{13}N-ammonia in PET imaging did not result in different management and different long-term cardiac event-free survival, as compared with stress/rest ^{99m}Tc-sestamibi SPECT imaging. Although this study was not intended to compare PET and SPECT in a head-to-head fashion, when comparing the amount of normal, jeopardized and nonviable myocardium in all 103 PET and 103 SPECT uniform polar maps, no difference between the PET and SPECT groups was observed. We presume that this lack of difference is an important reason for not observing a difference in management and, more importantly, in cardiac event-free survival between the PET- and SPECT-based management groups.

To detect jeopardized myocardium, established criteria were used. For ^{99m}Tc-sestamibi, we used a 50% cutoff value of maximal activity criteria to optimize detection of jeopardized myocardium (36,38), and for ^{13}N-ammonia/^{18}FDG PET imaging, we used mismatch and match criteria, as previously described by Blanksma et al. (33). If ^{99m}Tc-sestamibi SPECT in our study had substantially underestimated viability, as compared with ^{18}FDG PET, then patients randomized to ^{99m}Tc-sestamibi SPECT–based management were expected to be treated with drugs more frequently and to show high event rates, as reported in drug-treated patients exhibiting jeopardized myocardium (12–14,39). Moreover, the event rates in the drug-treated patients randomized to ^{99m}Tc-sestamibi SPECT would have been higher than those in the drug-treated patients randomized to ^{13}N-ammonia/^{18}FDG PET. In our study, this was not observed. In fact, the drug-treated patients in both the ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT groups demonstrated event rates consistent with an absence of residual jeopardized myocardium, as reported in prognostic ^{18}FDG studies (12–14,16,20). Ideally, only patients exhibiting jeopardized myocardium would be revascularized, accompanied by a relatively low event rate at long-term follow-up. The revascularized patients randomized to ^{13}N-ammonia/^{18}FDG PET showed relatively low event rates, in agreement with published data (12–14,16,20), and the event rates of revascularized patients randomized to ^{99m}Tc-sestamibi SPECT were not different. Thus, the prognostic value for event rates of ^{13}N-ammonia/^{18}FDG PET–based management is consistent with previous data, and the ^{99m}Tc-sestamibi SPECT event rates are not different.

In our study, we did not discriminate between ischemic myocardium and nonischemic but viable myocardium. Both PET and SPECT perfusion imaging were performed with pharmacologic stress. For PET imaging, the combination of stress perfusion with ^{18}FDG permits the identification of hibernating myocardium, as well as stress-induced ischemia (21). For ^{99m}Tc-sestamibi SPECT, jeopardized myocardium was identified by detecting both ischemic and nonischemic but viable segments, by using reversibility criteria and 50% of maximal tracer uptake. As suggested by Bonow (40) and applied in the present study, jeopardized myocardium should be revascularized because both hibernating myocardium and stress-induced ischemia may benefit from it.

Study limitations. This study was designed to provide more insight on clinical relevance of assessment of jeopardized myocardium in terms of prognosis, as suggested by Bonow (40). Therefore, no data on functional status of patients were obtained during follow-up, and the interesting relation between functional outcome and prognosis remains unexplored in the present study. Patency after revascularization was only assessed when indicated clinically, because this study was designed to evaluate patient management in a practical clinical setting. Although all patients in our study had wall motion abnormalities, ~35% of all them had left ventricular ejection fraction <30%. Because this is a relatively small number, the applicability of the present results for this specific group needs further study. Eight patients did not receive the intended treatment, two of whom died before they were revascularized. The remaining six patients experienced no cardiac events during follow-up; however, it appears that more patients in the SPECT group (n = 5) did not receive the intended treatment, as compared with those in the PET group (n = 1). In three patients, the decision to treat differently than intended had no relation to the randomized technique. For the remaining three treatment changes, we could not identify whether they were due to either false positive or false negative imaging results, because this study provided no gold standard. Nevertheless, these changes from intended treatment illustrate that the clinical condition of the patients remains important to treating physicians in clinical practice.

Study implications and conclusions. Patient management based on identification of jeopardized (i.e., ischemic or viable) myocardium with ^{13}N-ammonia/^{18}FDG PET and stress/rest ^{99m}Tc-sestamibi SPECT imaging does not result in different cardiac event-free survival and different patient management in patients who are candidates for revascularization with suspicion of jeopardized myocardium. Our results demonstrate that both ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT imaging accurately identified patients who should be revascularized or treated with drugs, based on the presence or absence of jeopardized myocardium. Therefore, both ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT imaging may be used for determination of patient management in a clinical setting.

The previously reported (28) differences in sensitivity and specificity between ^{13}N-ammonia/^{18}FDG PET and ^{99m}Tc-sestamibi SPECT for recovery of left ventricular function were not reflected in a different prognosis, neither in the total study group nor in the specific subgroups. Further studies are needed to evaluate the accuracy of other viability detection techniques in patient management in terms of prognosis. Moreover, the relation between left ventricular functional recovery and prognosis should be explored, as recovery of function might not be the sole factor influencing prognosis (41).

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